

Eight Years Follow-up After Rush Specific Oral Tolerance Induction to Cow's Milk Proteins

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Abstract

Cow's milk allergy (CMA) has a great impact on children and families quality of life. Recent studies point to a tendency for longer duration and greater severity. Specific oral tolerance induction (SOTI) to cow's milk (CM) has been regarded as a promising strategy to improve care of these patients, but prospective data concerning tolerance and safety after ending SOTI are still lacking. The longest follow-up reported had the duration of 4 years. We report a case of a young male, now aged 20 year-old, with persistent CMA, successfully submitted to a rush SOTI CM protocol, which kept CM tolerance after 8 years. During this time he maintained daily CM ingestion and strictly followed doctor's instructions. With a faster and easier to perform protocol we achieved the same efficacy as those reported before. The key to success could be the regular exposition to allergen. Publishing these case reports reinforces the safety and efficacy of SOTI therapeutic strategy.

Keywords: Anaphylaxis; Cow's milk allergy; Follow-up; Oral tolerance induction; Protocol; Up-dosing; Weekly schedule

Background

Cow's milk allergy (CMA) affects approximately 2.5% of children during the first years of life [1]. The prevalence of food allergy, and of CMA in particular, is believed to be

increasing [2, 3]. Although in the past it was believed that the majority of cow's milk (CM) allergic children tolerated it until school age, recent studies point to a much more delayed resolution [4]. Avoidance diet in CMA is particularly difficult since milk is a ubiquitous food; also, the fear of an inadvertently ingestion of hidden CM with occurrence of a severe reaction has a great impact on children and families quality of life [5]. Therefore, specific oral tolerance induction (SOTI) to CM has been regarded as a promising strategy to improve care of these patients.

In several research clinical trials, a few sublingual and oral protocols have been found to be generally well-tolerated and safe in highly controlled clinical settings [6]. Prospective data, however, concerning tolerance and safety after ending SOTI are still lacking. The longest follow-up published, by Meglio et al, included 4 years and 8 months [7]. Publishing these case reports reinforces the safety and efficacy of SOTI therapeutic strategy.

We describe herein an 8 years follow-up after successful SOTI to CM.

Case Report

A Caucasian young male, now aged 20 year-old, was referred to Immunoallergy Department in 2001, at the age of 10 years, due to CMA diagnosed in the 1st month of life. He was breastfed until the 14th day of life and then initiated a CM infant formula. Two days later, about 30 minutes after each meal, he started reproducible episodes of generalized urticaria, ocular angioedema and vomiting. He was admitted to hospital and started a soy formula with good tolerance, which has kept throughout these years. During childhood he had several episodes of accidental ingestion of hidden CM, the last at the age of 8 year-old. He also reported moderate asthma, controlled with formoterol and budesonide, rhinitis controlled with mometasone, and a prior history of atopic eczema until 4 year-old. Family history was also positive for atopy.

The allergy workup performed included skin prick tests (SPT) (Laboratorios Leti[®], Madrid, Spain), which were positive to house dust mites and grass pollens, as well as

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Table 1. Evolution Throughout the Years of Total (IU/L) and Specific IgE (kUA/L), and Skin Prick Tests (mean wheal)

	2001	2003	2004	2005	2007	2010
Total IgE	231	199	235	172	145	124
Whole Cow's milk						
sIgE	1.2	12.3	9.0	0.5	ND	Neg
SPT (mm)	8.5	ND	Neg	Neg	Neg	Neg
Casein						
sIgE	2.8	5.2	6.4	2.1	ND	Neg
SPT (mm)	8	ND	8	3	Neg	Neg
α -lactalbumin						
sIgE	2.6	9.4	14.0	0.4	ND	Neg
SPT (mm)	8	ND	Neg	Neg	Neg	Neg
β -lactoglobulin						
sIgE	0.9	3.9	1.4	Neg	ND	Neg
SPT (mm)	7.5	ND	9.5	3	Neg	Neg

ND: Not done; Neg: Negative; mm: milimeters; sIgE: specific IgE; SPT: skin prick tests.

for whole CM, casein, α -lactalbumin and β -lactoglobulin and so were specific IgE (ImmunoCAP[®], Phadia, Uppsala, Sweden) (Table 1).

An open oral food challenge (OFC) was performed, and severe anaphylaxis occurred with the cumulative dose of 76 mL. At the age of 12 years, OFC was positive with 38 mL.

Because of this persistent CMA confirmed by stably positive OFCs, in 2003, with 13 year-old, a SOTI to CM was proposed, after detailed explanation about risks and advantages to him and his parents. The SOTI lasted 2 weeks, starting with increasing doses, reaching 30 mL on the first day, and with daily progressively increases in hospital setting, until a single dose of 200 mL of CM could be tolerated. The protocol was completed with mild side effects (1 episode of facial urticaria, controlled with cetirizine 10 mg and 1 episode of abdominal pain, self-limited) and no severe systemic reactions.

He was advised to keep a daily ingestion of at least 200 mL of CM, always after a meal, and without vigorous exercise in the 2 subsequent hours. Regular appointments with medical staff were programmed and until now, 8 years after SOTI, no reactions had occurred. Also, he is currently free of asthma and rhinitis symptoms, and therefore without therapeutics. Throughout the years, specific IgEs and SPT results for whole milk and CM proteins decreased, until reaching total negativity (Table 1).

Discussion

Our patient was submitted to a SOTI protocol different from that reported by Meglio et al [8], but also an excellent tolerance was observed at the end of 8 years, as long as he kept CM ingestion. Similarly to what was reported by Meglio et al at 4 years follow-up, an improvement occurred in what concerns to asthma and rhinitis [7]. sIgEs and SPT decreased until reaching negativity. We prove that this protocol is equally effective and safe, with the advantage of being less time consuming and consequently more convenient, therefore representing an alternative. Spreading the safety and efficacy of SOTI strategy provides current knowledge on this issue and improves confidence of allergists to start using more often this therapeutic, which clearly improves quality of life of these patients and their families, and additionally seems to be beneficial to other concomitant allergic diseases. Recent studies suggested that it should be seen as a first line approach therapy for CM allergic patients and should be applied earlier in life [9], in order to obtain the maximum benefit regarding the number of ages free of CM allergy and avoid that age contributes as a factor for lower success rates.

The essential key to success seems to be, as reported by Rolinck-Werninghaus et al, the maintenance of regular ingestion [10], and that should always be emphasized to patients. Since until now dosage intervals needed for the

maintenance phase to preserve the acquired tolerance are not defined, daily ingestion seems to be the best strategy.

Conflicts of Interest

None.

Funding Source

None.

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